REMARKS

Claims 70, 74-90 and 93 are currently pending in the application. Claims 81-83, 85-88 and 90 are withdrawn from consideration by the Examiner. Claims 78 and 89 are amended. Claim 94 is newly added. The amendments find support in the specification and are discussed in the relevant sections below. No new matter is added.

Claim Rejections 35 USC § 112 first paragraph

Claims 78-79 are rejected under 35 U.S.C. 112, first paragraph, because the Office action asserts that the specification, while being enabling for a host cell in culture comprising a polynucleotide with the sequence as set forth in SEQ ID NO:1, encoding SEQ ID NO:2, does not reasonably provide enablement for in vivo transfection. The Office action asserts that the instant claims are not enabled because Applicant's disclosure does not address any of the methods necessary to make a host cell in an animal which comprises the polynucleotide of interest. The office action also cites an article by Eck and Wilson (1996) which is described in the office action as reporting that "numerous factors complicate in vivo gene expression which have not been shown to be overcome by routine experimentation", and directs one's attention to page 81, column 2, second paragraph, to page 82, column 1, second paragraph, of the article.

Applicant notes the referenced section of the article is entitled "Obstacles to Gene Therapy" and refers to "clinical efficacious therapies" (see page 81, column 2, lines 10-13). However, Applicant is not claiming a method of human gene therapy, but is claiming a host cell which comprises the polynucleotide of interest. In order to clarify Applicant's invention, Applicant has amendment claim 78 to recite "An isolated host cell comprising the vector of claim 77". Because the office action states that the specification is enabling for a host cell in culture comprising a polynucleotide with the sequence as set forth in SEQ ID NO:1, encoding SEQ ID NO:2, Applicant contends that the rejection of claim 78 can properly be withdrawn in view of said amendment.

Applicant has added new claim 94, which recites "A host cell comprising the vector of Claim 77, wherein said host cell is comprised by a transgenic non-human mammal." Support for newly added claim 94 is found on page 6, lines 20-32 and page 7, lines 1-8 of the specification,

which discloses that the present invention concerns a transgenic non human mammal over expressing (or expressing ectopically) the nucleic acid molecule encoding the receptor according to the invention, that the present invention also concerns a transgenic non human mammal comprising a homologous recombination knockout of the native receptor according to the invention, and that preferably, the transgenic non human mammal is a mouse.

Newly added claim 94 encompasses a host cell in non-human transgenic animals. Pertaining to the Office action's assertion that Applicant's disclosure does not address any of the methods necessary to make a host cell in an animal which comprises the polynucleotide of interest, Applicant contends that because methods of making transgenic animals are well known, Applicant is not required to disclose detailed methods. "The specification need not disclose what is well-known to those skilled in the art and preferably omits that which is well-known to those skilled and already available to the public." *In re Buchner*, 929 F.2d 660, 661, 18 USPQ2d 1331, 1332 (Fed. Cir. 1991); *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986), *cert. denied*, 480 U.S. 947 (1987); and *Lindemann Maschinenfabrik GMBH v. American Hoist & Derrick Co.*, 730 F.2d 1452, 1463, 221 USPQ 481, 489 (Fed. Cir. 1984).

Further, the MPEP in Section 2164.03 teaches "The amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art. *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). The 'amount of guidance or direction' refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to be explicitly stated in the specification".

In the instant case, Applicant contends that techniques for making and using transgenic non-human animals such as mouse were well known at the time the invention was made. The instant specification exemplifies the cloning of SEQ ID NO:1 into a vector which expresses the encoded protein SEQ ID NO:2 and its transfection into the mammalian cell 1321N1 cell, see

parts 1-3 of the Results Section of the specification. By virtue of this exemplification of in vitro expression in mammalian cell lines, and in view of the well known techniques of making transgenic animals, Applicant contends that the instant specification provides sufficient guidance for one of skill in the art at the time the invention was made, to make and use a transgenic animal with a host cell comprising the recited nucleic acid molecule.

With respect to the Office Action's assertion that in human gene therapy, "numerous factors complicate in vivo gene expression which have not been shown to be overcome by routine experimentation", Applicant contends that though said "routine experimentation" involved in in vivo gene expression is generally not acceptable in human therapy, such experimentation is routine and acceptable in non-human transgenic animals, such as mice. The preponderance of such transgenic animals, and their substantial use as models of human disease, are evidence that experimentation involving host cells of non human mammals, such as mice, is routine. Therefore, Applicant submits that making and using a host cell comprising a gene of interest wherein said host cell is comprised in a non-human mammal such as mouse is routine. Accordingly, the specification, with its exemplification of in vitro transfection and subsequent expression in mammalian cell lines of the nucleotide recited in claim 94, when combined with the well established technology of transgenics, is enabling for a host cell which is comprised by a transgenic non-human mammal

Claim Rejections 35 USC § 112 second paragraph

Claim 89 is rejected under 35 U.S.C. 112, second paragraph, because the Office action asserts that the preamble and the conclusion of claim 89 do not correlate, and as such the metes and bounds of the claim are unclear.

Applicant traverses the rejection. However, in order to more clearly define the claimed invention, Applicant has amended the conclusion of claim 89 to read "detecting the presence of any such ligand bound specifically to said receptor, thereby determining if the ligand can specifically bind said receptor". In view of said amendment, reconsideration and withdrawal of the rejection is respectfully requested.

Claim Rejections 35 USC § 102

Claims 70, 74-75, 77-79, 84 and 89 are rejected under 35 U.S.C. 102(a) as being anticipated by Nguyen et al. (1995).

Applicant traverses the rejection on the grounds that Ngyen, which was published in December of 1995, is not prior art. The instant application is a 371 application of PCT/BE96/00123 filed 11/21/1996, which claims priority to EPO 95870124.5 filed 11-21-1995 in English. Because the referenced art was published after the filing date of Applicant's earliest priority document, the referenced art does not anticipate the invention recited by the instant claims.

The certified copy of EPO 95870124.5, which is in English, should have been received by the USPTO from the International Bureau (PCT Rule 17.2(a)). Therefore, reconsideration and withdrawal of the rejection is respectfully requested.

Allowable Subject Matter

Applicant acknowledges the statement in the Office Action that Claims 76 and 93 are allowable.

Conclusion of Office Action

In the Conclusion section of the Office Action it is stated that claims 70, 74-75, 78-79, 84 and 89 are rejected. However, Applicant notes that claim 80 was not listed in the office action as being either allowable or rejected, and also notes that no rejections were applied to claim 80 in the office action. Applicant further notes that claim 80 is not indicated as being allowed or rejected in the office Action Summary Form PTO-326, although it is indicated as being pending. Applicant respectfully requests clarification on the status of claim 80.

Applicant submits that all claims are allowable as written and respectfully requests early favorable action by the Examiner. If the Examiner believes that a telephone conversation with Applicant's attorney/agent would expedite prosecution of this application, the Examiner is cordially invited to call the undersigned attorney/agent of record.

Respectfully submitted,

Date: 10/22/03

Elizabeth M. S Reg # 45,128 for

Name: Kathleen M. Williams
Registration No.: 34,380
Customer No.: 29933
Palmer & Dodge LLP
111 Huntington Avenue
Boston, MA 02199-7613
Tel. (617) 239-0100